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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Arne Elof Brandstrom

Serial No. : 640,020 Examiner: J. Fan

Filed : August 10, 1984 Group Art Unit: 121

For : NOVEL COMPOUNDS

DECLARATION UNDER RULE 132

Hon. Commissioner of Patents and Trademarks

Washington, D.C. 20231

S I R :

I, Arne Elof Brandstrom, declare that:

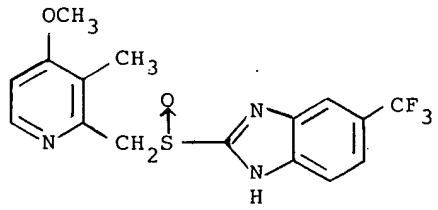
1. I am a citizen of Sweden residing at Anders Mattsonsgatan 13B, S-415 06 Goteborg, Sweden.

2. I was awarded the degree of Doctor of Philosophy in Organic Chemistry from the University of Uppsala in 1952.

3. I have been employed by AB Hassle, since 1959, and have held the position of Senior Scientist since 1967. I am an author or co-author of more than 100 publications on organic chemistry, medicinal chemistry, biochemistry, analytical chemistry and physical chemistry.

4. I am the inventor of the invention disclosed in U.S. Patent Application Serial No. 640,020, and I am familiar with the Official Action dated January 2, 1985 in which the Examiner rejected all claims. I understand that the base addition salts of the present application are alleged to be obvious in view of U.S. Patent No. 4,472,409 of Senn-Bilfinger.

5. I have tested the solution stability of sodium omeprazole and the sodium salt of the compound of the formula



which is disclosed in the Senn-Bilfinger patent. Solution stability is necessary for a compound to have utility for intravenous administration, an intended use of sodium omeprazole.

6. The sodium salts of the two compounds were dissolved in aqueous buffer solution. The solutions had a final pH of 9.02. The solutions were stored at 37°C and samples were periodically taken and analyzed by HPLC to determine the content of undegradated material. First order rate constants and half-lives were calculated from the decrease in the concentration of undegradated material with time.

7. The results of these tests were as follows:

Test Substance	Rate Constant min^{-1}	$t_{1/2}$ (hr)
omeprazole, sodium salt	$(8.19 \pm 0.08) \times 10^{-5}$	141
trifluoromethyl derivative, sodium salt	$(2.21 \pm 0.02) \times 10^{-3}$	5.2

These results clearly show that sodium omeprazole is by far more stable than the sodium salt of the Senn-Bilfinger compound. This stability is significant since solutions of a drug must exhibit less than 1% degradation to be acceptable for injection. Sodium omeprazole solutions can be prepared as much as 2.05 hours before administration because of their stability, but the sodium salt of the Senn-Bilfinger compound would have to be administered within 4.5 minutes of preparation.

8. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent thereon.

Dated: July 4, 1985

Arne Elof Brandstrom

ARNE ELOF BRANDSTROM